

--IDENTIFICATION, PRODUCTION AND USE OF STAPHYLOKINASE
DERIVATIVES WITH REDUCED IMMUNOGENICITY AND/OR REDUCED
CLEARANCE

ABSTRACT OF THE DISCLOSURE

E1 Methods for the identification, production and use of staphylokinase derivatives characterized by a reduced immunogenicity after administration in patients and that can be administered by a single bolus injection. The derivatives of the invention are obtained by preparing a DNA fragment comprising at least part of the coding sequence of staphylokinase; performing *in vitro* site-directed mutagenesis on the DNA fragment; cloning the mutated DNA fragment in a suitable vector; transforming a suitable host cell with the vector; culturing the host cell under conditions suitable for expressing the DNA fragment; purifying the staphylokinase derivative and chemically modifying Cys residues with thiol-directed polyethylene glycol. The invention also relates to pharmaceutical compositions comprising at least one of the staphylokinase derivatives according to the invention together with a suitable excipient, for treatment of arterial thrombosis.--

IN THE SPECIFICATION:

On page 1, please insert the following heading after the Title.

E2

--BACKGROUND OF THE INVENTION--

On page 1, please insert the following heading after THE BACKGROUND OF THE INVENTION and before the first full paragraph that starts on line 5.

E3

--Field of the Invention--

On page 1, please insert the following heading after the first full paragraph and before the second full paragraph that starts on line 16.

E4

--Description of the Related Art--